

## To Study the Histopathological Variations of Non - Neoplastic Skin Lesions in a Tertiary Care Centre of Central Rajasthan

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Article Received:00-00-2025

Article Accepted:00-0-2025

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### ABSTRACT

**Background and Objective:** Skin lesions are a prevalent occurrence across the globe, yet their clinical appearance can vary significantly based on demographic factors and geographical regions. Accurate diagnosis is crucial since the management approach differs for each case. Therefore, histopathology serves as an indispensable tool for establishing a definitive diagnosis. The main objective of this study is to analyse the histopathological patterns of biopsy samples from non-neoplastic skin lesions.

**Material and Methods:** This prospective study was conducted at the Department of Pathology, J.L.N. Medical College, and its affiliated hospitals in Ajmer, from July 2022 to December 2023. A total of 200 patients were enrolled whose skin biopsy samples exhibited clear indications of specific non-neoplastic conditions. Cases with insufficient or autolyzed skin biopsies were excluded from the study.

**Results:** In the current study of 200 cases, the average age of the sample was found to be 38.92 years. Among the participants, there were 84 females and 116 males. The nodule was the most common clinical lesion, accounting for 38% of cases. Epidermal keratinous cyst was the most frequent histopathological diagnosis (25%), followed by infectious disorders of the skin and subcutaneous tissue. Within the infectious disorders, leprosy was the most common subtype, representing 13.5% of cases. Histopathological diagnosis was consistent with clinical diagnosis in 177 cases (88.5%), with a kappa measure of agreement of 0.847.

**Conclusion:** The gold standard for diagnosing various skin lesions remains histopathological examination of skin biopsies. When combined with the patient's clinical history, it significantly contributes to the accurate diagnosis of the majority of skin conditions.

**Keywords:** Histopathology, Non-neoplastic lesions, Skin.

### INTRODUCTION

The integumentary system is the largest organ of the human body consisting of skin, hair, nails and related muscles and glands.<sup>1</sup> Skin consists of stratified cellular epidermis and underlying dermis of the connective tissue. The epidermis consists mainly of keratinocytes and is nearly 0.05-0.1 mm thick. The dermis is composed of collagen, elastic tissue and ground substance. A layer of subcutaneous fat is present below the dermis.<sup>2,3</sup>

Skin behaves as a protective cover against heat, light and injury. It acts as a thermoregulator and provides an innate immune defence against various infections.<sup>2</sup>

Skin problems are most commonly encountered among the health problems in India<sup>4</sup>. It varies from 4.2% to 11.6% in the general population<sup>5</sup>. Besides hot and humid climates, factors such as poor hygiene, limited access to water, overcrowding, and high interpersonal contact significantly contribute to certain skin conditions. These diseases often lead to considerable morbidity, manifesting as disfigurement, disability, or symptoms like persistent itching, which greatly reduce quality of life. They can also result in social isolation and impose economic burdens.<sup>6</sup>

The mutual relationship between clinical and histopathological diagnosis is frequently essential for establishing an accurate diagnosis. Early histopathological examination using Hematoxylin and Eosin stains, can help prevent subsequent opportunistic infections and complications.<sup>7,8</sup>

Dermatologists mostly rely on clinical diagnosis and rarely investigate further for confirmation. Nearly 1.3% patients presenting to dermatology OPD need biopsy.<sup>9</sup> Majority of the disorders are clinically restricted to a few features such as macule, papule, nodule, hyperpigmentation, hypopigmentation, vesicle, ulcer and some others, and this impedes the clinician to reach an accurate diagnosis hence, histopathology is essential for proper diagnosis and treatment.<sup>10</sup>

The biopsy technique is relatively simple, fast and done as an outdoor procedure with little inconvenience to the patient.<sup>11</sup>

Skin disorders can be classified into non-neoplastic and neoplastic disorders. The lesions are classified according to ICD-10 (International Classification of Diseases) for easy analysis.<sup>12</sup>

The main objective of the present study is at describing the histopathological spectrum of non-neoplastic dermatological disorders at Tertiary Care Institute in central Rajasthan

## MATERIALS AND METHODS

**Study Design** - This prospective study was conducted at the Department of Pathology, Jawaharlal Nehru Medical College and Associated Group of Hospitals, Ajmer (Rajasthan) from July 2022 to December 2023 after obtaining approval of the Institutional Ethics Committee.

**Inclusion criteria** - All skin biopsies that showed definite signs of any specific non-neoplastic pathology and patients of all age groups and both sexes were included in the study.

**Exclusion criteria** - Inadequate and autolysed skin biopsies and cases with neoplastic skin lesion/histology were excluded from the study.

**Method of collection of data:** A written informed consent was taken from all the patients included in the study and their detailed clinical history was then noted in the proforma. Specimens were surgical biopsies such as punch biopsy, shave biopsy, excision biopsy and incisional biopsy. Specimens were fixed in 10% neutral buffered formalin and were sent to histopathological section. Paraffin embedded sections were prepared and subjected to microtomy and then the slides were routinely stained with Harris Hematoxylin and Eosin (H & E) and special stains were done wherever necessary as per the standard protocols.<sup>28</sup> The sections were then studied microscopically. The data obtained was collected in a specially designed proforma for the study. It was then further subjected to statistical analysis.

## RESULTS

This prospective study was conducted over a period of one and a half years, from July 2022 to December 2023, comprising of 200 cases of non-neoplastic skin lesions. These lesions were classified according to their histomorphology. The findings were analysed and the final observations and results were tabulated. The following observations were made:

**TABLE 1: DISTRIBUTION OF NON-NEOPLASTIC SKIN LESIONS IN THE PRESENT STUDY**

S. No.	Group	Number of cases	%
1	Disorders of skin appendages	60	30
2	Infections of the skin and subcutaneous tissue	41	20.5
3	Other disorders of the skin and subcutaneous tissue	37	18.5
4	Bullous Disorders	31	15.5
5	Papulosquamous Disorders	26	13
6	Dermatitis and Eczema	5	2.5
	<b>Total</b>	<b>200</b>	<b>100</b>

The distribution pattern of non-neoplastic skin lesions in our study (Table 1 and 2) showed disorders of skin appendages to be the most common type of skin lesions, accounting for 30% (60 cases). Among this, the most frequently observed

disorder was the epidermal keratinous cyst, with 50 cases identified (25%). This was followed by 5 cases each of dermoid cysts and trichilemmal cysts. Additionally, there was one case of discordance where a lesion was clinically diagnosed as actinic keratosis, but histological examination revealed it to be an epidermal keratinous cyst.

The second most common was the infections of the skin and subcutaneous tissue with 41 cases (20.5%). In this group, Leprosy was the most common infectious disorder with 27 cases reported (13.5%). This was followed by 10 cases of lupus vulgaris, 2 cases of mycetoma, and 1 case each of actinomycosis and histoplasmosis. There were several instances of discordance in the diagnoses. One case of actinomycosis was clinically identified as a cyst but was histologically confirmed as actinomycosis. Another case of lupus vulgaris was clinically misdiagnosed as psoriasis. Similarly, histoplasmosis was clinically misdiagnosed as sarcoidosis, and two cases of mycetoma were clinically mistaken for dermoid cysts.

The third common group is the other disorders of the skin and subcutaneous tissue with 37 cases (18.5%). The most common disorder in this category is connective tissue disorder, with 14 cases reported (7%). This is followed by 8 cases of calcinosis cutis. Atrophic disorders and vasculitis each accounted for 3 cases. There were 2 cases each of atopic erythroderma and erythema nodosum. Additionally, there was one case each of cutaneous amyloidosis, idiopathic eruptive macular hyperpigmentation, lupus miliaris disseminatus faciei, striated keratoderma, and subacute cutaneous lupus erythematosus. Several instances of discordance were observed in the diagnoses. Two cases of calcinosis cutis were clinically identified as sebaceous cysts. Another case of morphea was mistakenly identified as nevus, and idiopathic eruptive macular hyperpigmentation was clinically misdiagnosed as lichen planus pigmentosus.

The fourth common group is the bullous disorders with 31 cases (15.5%), with pemphigus vulgaris as the most common disorder, with 15 cases reported (7.5%) and followed by 7 cases of bullous pemphigoid, 5 cases of pemphigus foliaceus, 3 cases of dermatitis herpetiformis, and 1 case of Hailey-Hailey disease. There were 6 instances of discordance in this category: Two cases of pemphigus vulgaris were clinically misdiagnosed—one as Stevens-Johnson syndrome and the other as linear IgA disease. Additionally, two cases of pemphigus foliaceus were misdiagnosed—one as subacute eczema and the other as psoriasis. Furthermore, one case of bullous pemphigoid was clinically identified as pemphigus foliaceus, and one case of dermatitis herpetiformis was mistaken for acute eruptive xanthoma.

The fifth common group is papulosquamous disorders with 26 cases (13%), In this category, psoriasis was the most common disorder, with 10 cases (5%). It was followed by lichen planus, which had 9 cases, and 3 cases of pityriasis lichenoides chronica. There were also 2 cases of pityriasis rubra pilaris and one case each of psoriariform reaction and pustular psoriasis. There were 7 discordant cases noted: Four cases of lichen planus were clinically misdiagnosed—one as actinic porokeratosis and three as psoriasis. Additionally, three cases of psoriasis were clinically misidentified—one as pemphigus foliaceus, one as leprosy, and one as seborrheic dermatitis.

The least common group in our study is the dermatitis and eczema group with 5 cases (2.5%). There was one case each of asteatotic eczema, atopic dermatitis, contact dermatitis, lichen simplex chronicus, and photoallergic contact dermatitis. There were no instances of discordance in this group.

In this study, the highest number of skin lesions, 38 cases (19%), were observed in individuals aged 31-40 years, followed by 33 cases (16.5%) in the age range of 41-50 years. Only 11 cases (5.5%) were identified in individuals younger than 10 years old.

**TABLE 2: DISTRIBUTION OF VARIOUS NON-NEOPLASTIC SKIN DISORDER ACCORDING TO HISTOPATHOLOGICAL DIAGNOSIS**

Group	Microscopic Feature	Number	Percent
Disorders of skin Appendages (n=60)	Epidermal Keratinous Cyst	50	60
	Dermoid Cyst	5	
	Trichilemmal Cyst	5	
Infections of the skin and subcutaneous tissue (n=41)	Actinomycetes	1	41
	Borderline Lepromatous Leprosy	4	
	Erythema Nodosum Leprosum	4	
	Histioid Leprosy	1	
	Histoplasmosis	1	
	Indeterminate leprosy	1	
	Lepromatous Leprosy	10	
	Lucio phenomenon	1	
	Lupus Vulgaris	10	
	Mycetoma	2	
	Borderline Tuberculoid Leprosy	1	
	Tuberculoid Leprosy	5	
Other disorders of the skin and subcutaneous	Atopic Erythroderma	2	37
	Calcinosis Cutis	8	

tissue (n=37)	Cutaneous Amyloidosis	1	
	Erythema Nodosum	2	
	Idiopathic eruptive macular hyperpigmentation	1	
	Lupus miliaris disseminatus faciei	1	
	Striated Keratoderma	1	
	SCLE	1	
	Atrophic disorders of skin	3	
	Vasculitis	3	
	Connective Tissue Disorder - Hypertrophic Scar	1	
	Connective Tissue Disorder - Keloid	5	
	Connective Tissue Disorder -Discoid Lupus Erythematosus	3	
	Connective Tissue Disorder -Morphea	5	
Bullous Disorders (N=31)	Bullous Pemphigoid	7	31
	Dermatitis Herpetiformis	3	
	Hailey hailey disease	1	
	Pemphigus Foliaceus	5	
	Pemphigus Vulgaris	15	
Papulosquamous Disorders (n=26)	Lichen Planus	9	26
	Pityriasis Lichenoides Chronica	3	
	Pityriasis Rubra Pilaris	2	
	Psoriariform reaction	1	
	Psoriasis	10	
	Pustular psoriasis	1	
Dermatitis and Eczema (n=5)	Asteatotic Eczema	1	5
	Atopic dermatitis	1	
	Contact Dermatitis	1	
	Lichen Simplex Chronicus	1	
	Photoallergic contact dermatitis	1	

**TABLE 3: SEX-WISE DISTRIBUTION OF NON-NEOPLASTIC SKIN LESIONS**

S. No.	Sex	Number	Percent	M: F Ratio
1	Male	116	58	1.3: 1
2	Female	84	42	
	<b>Total</b>	<b>200</b>	<b>100</b>	

Out of 200 cases of non neoplastic skin lesions, 116 (58%) were found in male and 84 (42%) were seen in female, resulting in a male-to-female ratio of 1.3:1 as shown in table 3.

**TABLE 4: CLINICAL PRESENTATION OF NON-NEOPLASTIC SKIN LESIONS**

S. No.	Clinical presentation	Number	%
<b>1</b>	<b>Nodule</b>	<b>76</b>	<b>38</b>
2	Plaque	43	21.5
3	Papule	13	6.5
4	Macule	12	6
5	Blister	16	8
6	Bullae	14	7
7	Patch	20	10
8	Pustule	1	0.5
9	Purpura	2	1
10	Ulcer	2	1
11	Scar	1	0.5
	<b>Total</b>	<b>200</b>	<b>100</b>

Based on the table 4, the most frequently observed clinical presentation was nodules, accounting for 76 cases (38%). This was followed by plaques with 43 cases (21.5%). Other presentations included patches, blisters, bullae, papules and macules.

The highest number of lesions occurred on the anterior trunk, accounting for 43 cases (21.5%), followed by 37 cases (18.5%) on the upper limbs, 27 cases (13.5%) on the lower limbs, 26 cases (13%) on the posterior trunk, 23 cases (11.5%) on the face, 21 cases (10.5%) on the scalp, 10 cases (5%) distributed across the entire body, 8 cases (4%) on the neck, and 5 cases (2.5%) on the genitalia.

**TABLE 5: CLINICO HISTOLOGICAL CORREALTION OF VARIOUS NON-NEOPLASTIC SKIN DISORDERS**

S. No.	Group	Number	%	Discordant
1	Disorders of skin Appendages (n=60)	60	30	1
2	Infections of the skin and subcutaneous tissue (n=41)	41	20.5	5
3	Other disorders of the skin and subcutaneous tissue (n=37)	37	18.5	4
4	Bullous Disorders (n=31)	31	15.5	6
5	Papulosquamous Disorders (n=26)	26	13	7
6	Dermatitis and Eczema (n=5)	5	2.5	0
	<b>Total</b>	<b>200</b>	<b>100</b>	<b>23</b>

This cumulative table illustrates, the discordance between clinical and histopathological diagnoses was seen in 23 cases, while 177 cases showed concordance between the two diagnostic methods. (Table 5)

**TABLE 6: SENSITIVITY AND SPECIFICITY OF NON-NEOPLASTIC SKIN DISORDERS**

S. No.	Groups	Sensitivity	NPV
1	Disorders of skin Appendages	98.33	99.29
2	Infections of skin and subcutaneous tissue	87.8	96.95
3	Other disorders of the skin and subcutaneous tissue	89.19	97.6
4	Bullous Disorders	80.65	96.57
5	Papulosquamous Disorders	73.08	96.13

Sensitivity and specificity were assessed for different groups. While sensitivity and negative predictive value varied among the groups, the specificity and positive predictive value were consistently 100% across all groups. Specifically, for the dermatitis and eczema group, all four metrics—sensitivity, specificity, positive predictive value, and negative predictive value—were 100%. Overall, the total accuracy for all cases was 88.5%. (Table 6)

**TABLE 7: MEASURE OF AGREEMENT**

		Value	Approx. Sig.
Measure of Agreement	Kappa	.847	0.0001
No. of Valid Cases		200	

Cohen's kappa ( $\kappa$ ) is 0.847, indicating the proportion of agreement over and above chance agreement. This value represents almost perfect agreement. Additionally, with a p-value of 0.0001, the kappa coefficient is statistically significantly different from zero. Therefore, we can conclude that our technique demonstrates almost perfect agreement as shown in table 7.

## DISCUSSION

In India, skin issues are a prevalent health concern, impacting approximately 4.2% to 11.6% of the population. In our study, we observed that the majority of skin lesions, accounting for 19% (38 cases), were found in individuals aged 31-40 years (the fourth decade). This finding was consistent with the results reported by Mathur K et al (2017)<sup>13</sup>, Gupta I et al (2019)<sup>14</sup> and Bisht M et al (2020).<sup>15</sup>

The present study reveals a slight predilection for males, with 58% of cases being male, resulting in a male-to-female ratio of 1.3:1. This observation is similar with the findings from Mukhopadhyay D et al (2020)<sup>16</sup> and Italia S et al (2022)<sup>17</sup>. In contrast, other studies such as Kumar V et al (2022)<sup>18</sup>, who reported a higher predilection among females. Since most patients at government hospitals come from lower socio-economic backgrounds, factors such as illiteracy, occupation, and social inhibitions may contribute to the lower reporting of cases among females in most of the regions in India.

The most common clinical presentation in our study was nodule, observed in 76 cases (38%). This result differs from the findings reported by Veldhurthy et al. (2015)<sup>19</sup>, Bajaj P et al. (2019)<sup>20</sup>, Bisht M et al. (2020)<sup>15</sup>, and Shehwar D et al. (2021)<sup>21</sup>. The classification of epidermal keratinous cysts—whether as non-neoplastic or benign lesions—remains a topic of ongoing debate. While some experts view them as benign, others classify them as non-neoplastic. In our study, we have categorized these cysts as non-neoplastic. They emerged as the most common lesion observed in our research and typically present clinically as nodules, differing from findings reported in other studies.

The most common non-neoplastic skin lesion was identified as Cutaneous Cyst (a disorder of skin appendages), accounting for 30% of cases. This finding aligns with the observation made by Albasari MA et al (2019)<sup>22</sup>, Ndukwe OC et al (2021)<sup>23</sup>, Deepti KN et al (2020)<sup>24</sup>. However, Mathur K et al (2017)<sup>13</sup> reported infectious diseases as the most frequent non-neoplastic lesions, while Bharti KS et al (2019)<sup>25</sup> found vesicobullous lesions to be the most common. This discrepancy may be attributed to variations in the occurrence of skin diseases based on geographical location, as well as the influence of racial, environmental, and socioeconomic factors within different populations.

The incidence of leprosy (an infectious disease) in our study was 13.5%, which aligns with the findings of Vijayshankar et al (2020)<sup>26</sup> and Kumar V et al (2022)<sup>18</sup>. Our study differs from the ones conducted by Bajaj P et al (2019)<sup>20</sup> and Mukhopadhyay et al (2020)<sup>16</sup>, which may be attributed to variations in community health practices or a lower number of patients visiting the outpatient department. This lower attendance might be due to a lack of awareness about the disease, potentially leading to an underreporting of cases.

In our study, the incidence of bullous disorders was 15.5%, which is similar with the findings of Shehwar D et al (2021)<sup>21</sup>, Kumar V et al (2022)<sup>18</sup> and Bharti S et al (2021)<sup>27</sup>. In our study, among bullous disorders, pemphigus vulgaris is the most common, with 50-60% of patients presenting with oral lesions. In some instances, mucosal lesions may be the sole symptom of the disease. Therefore, the diagnosis of pemphigus vulgaris should be considered for any patient with persistent oral erosive lesions.

The incidence of papulosquamous disorders in our study was 13% which is similar to the study of Bisht M et al (2020)<sup>15</sup> Albasri AM et al (2019)<sup>22</sup>. The most common among this is psoriasis which is approximately equal in males and females and occurring mostly on knees and elbows.

In our study, 200 cases were histologically examined. Of these, 177 cases were consistent with the clinical diagnosis, while 23 cases showed inconsistencies with the clinical findings. So, the clinicopathological concordance was seen in 88% of cases, which is comparable to the findings of Mathur K et al. (2017)<sup>13</sup>, Gupta I et al. (2019)<sup>14</sup>, and Bajaj P et al. (2019)<sup>20</sup> and Vijayshankar S et al (2020)<sup>28</sup>

## Conclusion

Non-neoplastic skin lesions cover a diverse array of conditions, although they are relatively limited in number. These lesions usually exhibit minimal changes, such as hypopigmentation, hyperpigmentation, macules, papules, and nodules, among others. To accurately diagnose and initiate the correct treatment, a skin biopsy is crucial and is regarded as the gold standard for diagnosing these different non-neoplastic skin lesions.

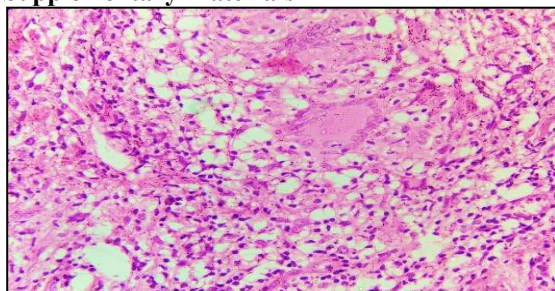
A skin punch biopsy is a quick, simple procedure that can be performed in an outpatient setting with minimal inconvenience to the patient. It is generally well-tolerated and usually leaves no noticeable scar.

Therefore, a collaborative approach between dermatologists and pathologists, supported by ongoing communication, can significantly enhance diagnostic accuracy, optimize patient management, and alleviate the burden of disease, ultimately improving patients' quality of life. The correlation between pathologists and dermatologists was notably high, at 88%.

**Conflicts of Interest** - None

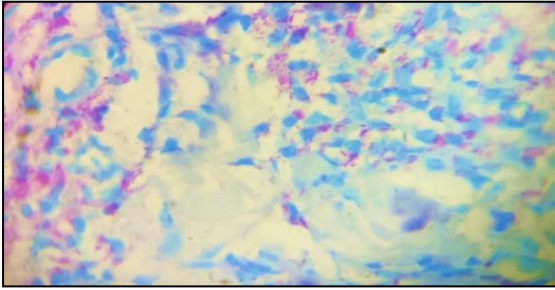
**Funding Statement** – None

**Supplementary Materials**

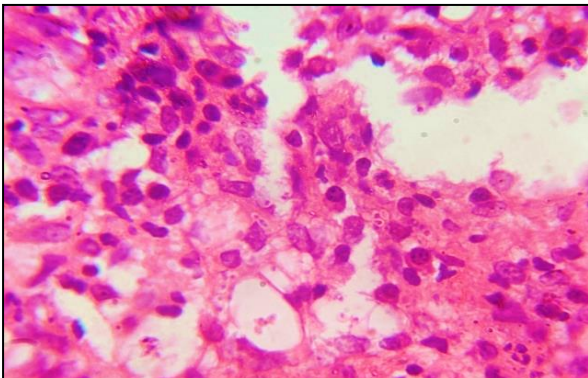


TUBERCULOID LEPROSY: (H&E  
stained under 40X)

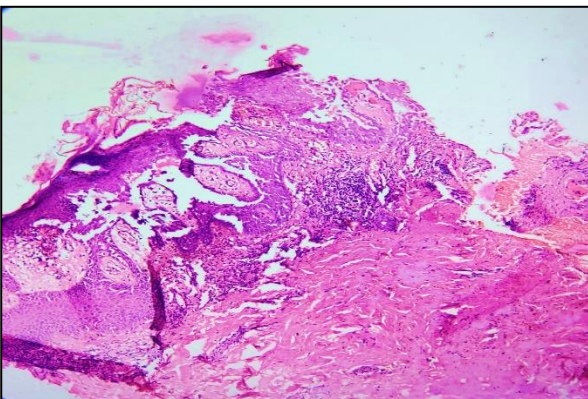




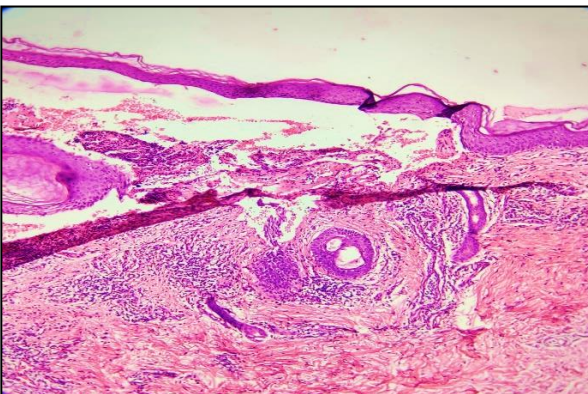
Modified Ziehl-Neelsen stained section seen under oil immersion: showing presence of acid-fast bacilli, in a case of leprosy.



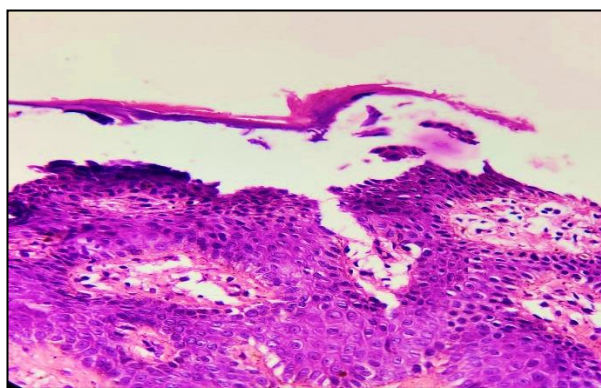
HISTOPLASMA: H & E stained seen under oil immersion lens



HAILEY HAILEY DISEASE: H&E stained under 10X



BULLOUS PEMPHIGOID: H&E stained under 10X



PEMPHIGUS FOLIACEUS: H&E stained under 40X.

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